

with the author's kind regards

ON THE

(4)

CALABAR BEAN:

ITS

ACTION, PREPARATIONS, AND USE.

BY

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ONE SHILLING.

THE CALABAR BEAN.

IN a paper published in *THE LANCET*, of July 18th, 1863, in which I called attention to the employment of the Calabar Bean in wounds of the cornea where there is prolapse of the iris, I mentioned that I had experimented with the bean, and not improbably should give the result. This I now propose to do. At the meeting of the British Medical Association, held at Bristol this year, I gave a paper on the subject, in which I related a few experiments ; but, as being more suitable to the occasion, dwelt rather upon the general results than explained the individual experiments upon which the deductions were founded. At the meeting of the British Association for the advancement of Science, lately held at Newcastle, I also introduced the subject in the Physiological Section. I think it right to others as well as to myself to mention this, inasmuch as it is possible some of the experiments I shall relate may be found to resemble those performed by other investigators with whom I have not had any communication. However this may be, the coincidence is merely that which is likely enough to arise when independent observers are engaged upon similar inquiries. Though the details of my experiments may not have appeared before, the general results have been publicly stated, and the greater number of the experiments were made prior to some which have since appeared.

It is not my intention to enter upon a geographical, historical, or botanical disquisition of the vegetable, which more than one writer has already fully given. I would merely say that we are mainly indebted to Professor Christison for calling attention to the bean in a paper read before the Royal Society of Edinburgh in 1856, in which he described the serious symptoms produced in himself by swallowing twelve grains of the bean, and gave a sketch of the character of the plant and its fruit, as well as the mode of using it as an ordeal for accused persons in the kingdom of Old Calabar, whence it is obtained, as related to him by a missionary, Mr. Waddell, who had repeatedly seen it publicly administered with fatal result, and who first brought the bean under the notice of Dr. Christison.

Though at that time nothing more than the highly poisonous property of the bean was established, the bold experiment of Dr. Christison on himself may be regarded as having indirectly led to the recent discovery of its curious power of contracting the pupil; for attention being thereby excited, Dr. Fraser commenced an investigation into the properties of the bean, and its action upon animals. In the course of which, while trying the poisonous effects produced by the extract of the bean, when applied to the different tissues of the body, he first noticed that on being introduced within the eyelids, contraction of the pupil soon followed; a result which of course would not have been anticipated, but which being observed, has opened up an interesting field for observation and enquiry.

Leguminous plants are notoriously very difficult of analysis, and this one appears to be particularly so. That in the laboratory of Dr. Christison, if it be possible, the active principle will be eliminated, no one can doubt, for in none more suitable could it be placed. I have had no intention of seeking to solve the question. Knowing in whose hands the matter is, had I been able I should not have attempted it; but the experiments which I shall relate as having been undertaken to determine the best solvent of the active principle of the bean will show that, whatever it be, it is not acted on in the manner the active proximate principle of plants usually is. It is to Dr. Christison's liberality, I believe, that most of those who have prepared extracts and tinctures have been indebted for the bean itself. For my own part, I wish publicly to declare my great obligation to him for the present of so large a proportion of his carefully accumulated stock, as has enabled me to experiment to the extent I have done. Also to Mr. Squire, of Oxford Street, London, I am indebted for a liberal supply of a tincture and a saturated paper prepared by him.

I propose to arrange what I have to say under three heads:—

1st. The effect of the bean when administered internally, in single doses, in repeated doses, and in combination with strychnia, the physiological action of which has been alleged to be antagonistic and neutralizing to that of the Calabar bean.

2nd. What is the best solvent for the active principle of the bean.

3rd. The effect upon the eye when locally applied, and how it may be most conveniently used in practice.

Before speaking of its action when taken internally, as many of the readers of *THE LANCET* may not have seen a description of the bean, and fewer still the bean itself, I cannot do better than quote that given of it by Dr. Christison, in the paper before referred to. He says—"It has a hard, brittle, and ligneous tegument, rather rough, and of a brownish-

crimson, or pale chocolate-brown colour; but many specimens are ash-grey, apparently from slight mould. The kernels, which weigh from thirty-six to fifty grains, are always in good preservation, and never injured in the slightest degree by insects—a rare occurrence with tropical seeds. They are white and hard, and may be chewed, and they have the taste of the eatable leguminous seeds, without bitterness, acrimony, aroma, or any other impression on the organ of taste—in fact, they are scarcely, if at all, distinguishable in taste from a haricot bean. This is a formidable peculiarity, were it possible for the seed to become a familiar poison in Europe. So far as I know, the property in question is peculiar to it; for all other poisonous seeds of the Leguminosæ, with which we are sufficiently acquainted, are bitter. The blandness of its taste is indeed of so unusual a character, that I was at first misled, and imagined that I had probably got a wrong and harmless seed; but I soon found that I was much mistaken.”

I may mention that some of the seeds presented to me by Dr. Christison are nearly black externally, and though, as described, for the most part white internally, in at least two the kernel has been brown in colour, without apparently affecting the active property of the bean. I find the externally darker-coloured beans to have a decidedly greater specific gravity than the lighter coloured, and to be for the most part larger in size; the internal hollow space is not so great. They are, I apprehend, the more matured fruit, but whether there be any difference in the activity of the two I am not prepared to say. We must await a larger supply before such a point can be determined. One of the entire beans weighed nearly ninety grains, others only a few grains less, and some not more than forty grains. In a bean which weighed seventy-five grains the hard husk weighed, when carefully separated from the kernel, twenty-four grains. The husk I believe to be altogether inert. Given to an animal, it induced no more effect than the little adhering kernel, which it is very difficult absolutely to separate, would cause. Though there is comparatively little or no taste, yet upon my palate and fauces a faint sensation of pungency, of the character, but infinitely less than capsicum, is left; and a disagreeable feeling of nausea and sinking is speedily induced when a small portion is carefully masticated and swallowed—for after the narrative of Dr. Christison's condition I have not ventured to swallow many grains at once. When fresh broken, the faint odour is not unlike that of a common horse-bean. One gentleman thought it resembled the odour of cantharides. If boiling water be poured upon the powdered bean the smell becomes very perceptible—of a leguminous seed, with slight pungency, and an aroma which is particularly objectionable to animals. It is also proper to remark that,

insipid as it is, animals have the greatest repugnance to swallowing it. Though the media in which I have given it were as likely as anything I could devise to be palatable to hungry creatures, most of them would reject meat or milk which contained it, even though they had been kept twenty-four or thirty-six hours without food. In none of the many experiments which I have made with various substances—the strongest flavoured or most irritating—have I experienced greater difficulty in forcing animals to swallow them, than with the Calabar bean. They seem to have an instinctive perception of its noxious property. To cats especially it appears repulsive. It seems to irritate the whole buccal mucous surface, judging from the large quantity of thick mucus which at once is poured out—for it does not appear to me to be saliva alone. This salivary, however, soon ceases: after a few minutes it is not so profuse, and sometimes it disappears altogether. It obviously is dependent upon the local irritation, and not upon any property the bean possesses as an internal sialagogue; for if the powder, even in sufficient quantity to destroy life, can be conveyed into the stomach without touching the mouth, as by rolling it up in thin slices of meat and getting a hungry dog to bolt it without mastication, not the least increased flow of saliva is induced.

I should state here that I have purposely abstained from employing rabbits in these, as in most other of the toxicological and physiological investigations which I have made. They are so easily affected by many substances, and have so little tenacity of life, that—though very convenient to the experimenter from the ease with which they are procured and their harmlessness and almost unresisting submission to the operator—the employment of them has, in my opinion, led to serious errors in estimating the action of remedies and poisons upon man and other animals, from whose organization they are so far removed.* A cat will resist with impunity what would destroy many rabbits.

Taking the very decided effect of twelve grains of the bean upon Dr. Christison as a startling point, I gave the following quantities:—

* This is of especial importance where chemical analysis has afterwards to be made of the contents of the stomach. The enormous paunch of the rabbit always contains a large mass of vegetable matter and woody fibre, than which nothing could be devised more likely to realise the old adage of seeking for a needle in a bundle of hay. A mineral poison may be eliminated; a difficult vegetable poison is more likely than not to escape detection. No wonder that in a celebrated trial, a well known toxicologist stated that he could detect strychnia in only one or two out of the four rabbits which he declared he had poisoned, with a view to prepare him to give evidence at the trial, and therefore asserted that strychnia often could not be found even when it had caused death, but great wonder that a man may be liable to be hanged on such evidence.

1. To a hungry half-grown terrier dog twelve grains of finely powdered bean, placed between two bits of meat, were given, and then a morsel more meat, all of which was bolted without mastication. No salivation was induced, nor any effect, until forty minutes had elapsed, when he became weak, staggering, and inclined to lie down, but when induced to do so he would run about. He was perfectly sensible and free from pain. The pupils became somewhat, though by no means greatly, contracted. In two hours all effect had passed away, and the dog appeared perfectly well. The following morning he was as well and active as ever, the pupils being quite normal.

2. Two days afterwards, to the same young dog twenty grains of the powdered bean was given in meat as before. He was very chary in eating it, requiring to be coaxed to do so; and unless he had been starved I do not think he would have taken it. Not more, perhaps hardly so much effect was produced as with the twelve grains. He was able to run about, and continued cheerful. The pupils were rather, but not greatly, contracted. But little saliva or mucus was produced, and neither purging nor nausea.

3. To a small dog, thirty-five grains of a finely powdered bean mixed with a little butter was given; it had to be forced down the throat, as it resisted swallowing it as much as possible. Slavering was at once induced. In fifteen minutes he was weak and staggering, but still walking about; sick and retching, but not vomiting; no contraction of the pupils. In thirty minutes he lay down, and was indisposed to move. In sixty minutes he could stand with great difficulty, and when made to move, which he would not do unless obliged, he staggered and fell down from excessive weakness. When compelled to walk, the forelegs were jerked straight out forwards, and the hind backwards, with some spasm, which, however, was neither great nor long continued. He was perfectly conscious, but appeared giddy; he retched, only getting up a little frothy mucus; strained much, passing a little feces and some mucus; and the pupils had become decidedly contracted. He crawled into a corner, and fell soundly asleep. At five hours, when aroused, he was much better, though not steady on the limbs; the pupils were still contracted. In the evening, ten hours after swallowing the bean, he was perfectly well; the pupils were less contracted.

4. To the same dog, three days afterwards, he being and having been perfectly well, was given twenty grains of the maceerate from a bean which had been treated—1st, with cold ether; 2ndly, with boiling ether; and thirdly, repeatedly with boiling spirit; so that all possible by these media had been extracted. For sixty minutes little effect was perceived, when it became weak and staggering, and continued in much the same

condition for another hour, when the loss of power materially increased, and the pupils became moderately contracted. The effects now gradually passed away, and in four hours the limbs had to a great extent regained their power, the pupils being still somewhat contracted. The same evening, eight hours after taking the macerate, the dog was as well and active as ever; the pupils had become rather dilated.

5. The bark from a large bean was carefully separated from the kernel and finely powdered; it weighed twenty-four grains. This was mixed with a small quantity of fat and given to a young cat which had been kept without food for several hours. As the cat would not eat it, it was forced down the throat; but as it resisted as much as possible, and struggled very hard against it, some little was lost; about twenty grains were swallowed. A great deal of thick saliva or mucus was at once poured out, and the effect upon the palate seemed to be most disagreeable. Milk-and-water was shortly afterwards offered, which it began eagerly to lap; as this washed the adhering particles into the throat, the cat at once desisted, and could not be induced to take more. For an hour no effect was manifested, when it became disinclined to move, and when forced to walk, the *hind* legs were very slightly jerked backwards. The pupils were widely dilated. In an hour and a half, when forced to move, which it was still disinclined to do, it became excessively excited, running wildly about, and attempting to scratch and bite (I think from fear). There was now considerable slavering, and frequent straining, as though it would be purged, but it was not. No other effect whatever was induced, and on the following morning it was as well as ever. The slight effect produced was probably caused by some little of the kernel having adhered to the shell, as it is difficult completely to isolate this.

6. *Kernel of the Bean*.—Three days afterwards to the same young cat I attempted to give ten grains of the bean itself, mixed with fat; but it resisted so violently that not more than six grains could have been swallowed. Repeatedly put into the back of the mouth, it made the most persistent efforts not to swallow. There was at once a large flow of thick mucus. No symptoms were observed until forty minutes had elapsed, when it crouched into a corner, and when made to move became wildly excited and cross, and tried to get behind every object it could, as though in dreadful fear. In an hour and an half there was copious thick saliva draining from the mouth, with retching and suppressed efforts at vomiting, as though the nausea was intense; yet nothing was ejected. There was also some straining as for purging, but merely a nodule or two of feces passed. The limbs now were greatly affected; when made to move it started as though to run, but instantly fell, and

did so every two or three steps it took. It crawled to the wall, against which it lay as though even lying were too great exertion for its muscles. There was not so much jerking motion of the limbs as was observed in the dogs. All the senses appeared quite unaffected. The pupils, which at the commencement of the experiment were widely dilated, had now become less so, but by no means contracted. The cat now began to show less weakness, and at the end of two hours was considerably improved, but still wishful to lie still and sleep. The next morning the pupils were quite normal, and the cat in every respect well.

7. Two days afterwards, the cat having been perfectly well, I gave it as follows: Eight grains of the finely-powdered kernel were infused for two hours in four drachms of boiling water. A considerable portion of the bean was dissolved, a very thin muddy mucilage being formed; this had a slightly warm taste. With great trouble, from the resistance offered, I forced it down the cat's throat. Immediately a free flow of thick saliva was induced, but only for a few minutes, when it ceased. No effect was apparent for ten minutes, the cat sitting naturally, and purring when petted; then she became suddenly restless and excited, making a sudden dart for the empty fire grate, and up the chimney, whence she could not be withdrawn, and where at the expiration of two hours and a half she was left for the night. The following morning she was found in the room perfectly well, the pupils being natural.

8. To a young cat which four hours before had eaten a good meal of meat, (the only one for twenty-four hours,) twenty-two grains of the powdered kernel were given, mixed with a table-spoonful of cold water. It resisted so violently that only about seventeen grains could be swallowed. It slavered considerably for the first few minutes only. At ten minutes it had nausea and straining as if for a motion. It became frightened, and ran wildly about. At thirty minutes its limbs had become so weak that being put on a table it wanted to jump down, but could not, and lay with its head hanging over, until its weight caused it to fall on to the ground. It crawled a few steps to a wall, along which it lay its whole length, continuing powerless, but restless, frequently retching without vomiting, and often passing a single nodule of feces at a time. In an hour and a half it revived, moved better, and appeared as though it would recover. At two hours it became weaker and very irritable, trying, as well as its little strength would allow, to scratch and bite, though still, I think, from fear, as when firmly held, it appeared pleased and satisfied. It gradually got weaker, the respiration more imperfect, and the circulation very feeble, until two hours and a half, when it died. It continued perfectly sensible, and so far as could be judged, free from pain. The pupils were rather dilated than not during the whole time.

Post-mortem examination immediately.—Brain, spinal marrow, and their membranes perfectly normal. There was neither injection of the nervous substance, nor congestion of, or effusion amongst, the membranes. The stomach was half full of semi-digested food. The whole of the intestinal canal, including the rectum, was full of fæces. The entire mucous membrane was pale, natural, and free from irritation. The lungs were pale, and collapsed on the chest being opened; they were free from congestion; there was neither pleuritic nor bronchial effusion. All the four cavities of the heart contained a little blood, but none were distended; it did not pulsate when pricked. Twelve hours afterwards the muscles were firm, and exhibited the usual cadaveric rigidity; the ventricles had become contracted and empty. There was not a trace of morbid appearance.

9. To a kitten seven or eight weeks old eight grains of the powdered kernel were given in one drachm of cream. It resisted, but the whole was swallowed. As before, much thick saliva was, at first only, poured out. In five minutes it became very vicious and excited, running wildly about into every corner it could get. At the end of ten minutes it could not stand, but fell on its side, struggling hard to get up. At fifteen minutes it was purged; respiration became very slow and laboured; the extremities were now very feeble, the hind especially. For a while it struggled, though ineffectually, to get up with the fore legs, the hind ones being hardly moved. The pupils were not contracted. At twenty-five minutes it improved, acquired more power, and appeared recovering; but, though perfectly sensible, it soon fell off again, until, at the end of an hour and a half, it lay as though dead, the only sign of life being slow, hardly perceptible respiration. There was no motion in the limbs, nor, so far as could be felt, in the heart. When roused, there was a feeble motion in the fore legs. So far as such utter prostration would allow an opinion to be formed, it was sensible. It was very cold, and was wrapped in cotton wool. At the expiration of two hours it entirely ceased to breathe. Before death the pupils were less dilated, but by no means contracted.

Autopsy, twenty-one hours after death.—Rigidity quite as great as ever occurs after death from any cause. The pupils were dilated. There was literally no abnormal appearance. The stomach and all the intestinal canal, were full, pale, and natural; the lining mucous surface being perfectly free from irritation or injection. The lungs were pale and collapsed. There was neither pleuritic effusion nor bronchial mucus. The left auricle and ventricle of the heart were moderately contracted, without containing any blood; both the right cavities and venæ cavæ moderately distended with soft dark clot. The brain, spinal marrow, and their membranes, were perfectly normal in every respect.

10. A young but full-grown rat, which had been caught in a large wire trap, was kept twenty-four more hours without food, when ten grains of the powdered bean, mixed with a little bacon fat, was given to it. Immediately the rat rushed to the food, and eagerly ate a portion, but soon desisted, and would not eat more; water was offered, but refused. It then sat washing and trimming its coat very actively for five minutes, when it became very restless, making violent attempts to escape, and passing nodules of faeces. At fifteen minutes it became very weak, and soon fell helplessly on its side, making no efforts to get away or bite when handled. It then struggled hard, but not convulsively; and at twenty-five minutes died. So far as could be seen, the pupils were not contracted; but rats are not good subjects for observing this. Not more than two grains and a half of the bean was eaten.

Autopsy, twelve hours after death.—Brain, spinal marrow, and their membranes, perfectly normal. Lungs collapsed, not congested, and of a bright pale-scarlet hue. Heart moderately distended, with a little dark blood in all its cavities. The stomach contained only the little bacon fat and some frothy mucus; the intestines were nearly empty (evidently the rat had not eaten much for some time before death); there was neither congestion nor irritation in the mucous membrane. The liver was dark in colour, which I believe it often is in rats. There was no pathological condition whatever. The muscular rigidity was very considerable. In twelve hours afterwards the scarlet colour of the lungs had disappeared.

In order to ascertain the effect of moderate doses of Calabar bean frequently repeated, I performed the three following experiments:—

11. To a third-grown cat, which had been kept without food for a whole day, I gave two grains of the powdered bean in a little milk. She began to lap it, but immediately desisted, and was shut up without other food for the night. On the following morning the milk was untouched. Two grains were now offered, placed between two pieces of beef: only a small part was eaten. More milk was added to the first quantity, thinking that if more diluted it might be taken. At night both the meat and milk were found untouched. As the kitten had now been forty-eight hours without food, the attempt to make it by hunger eat the bean was useless. I therefore forced down the throat two grains mixed with cream, which was violently resisted. This quantity was given night and morning for three days, and then three grains night and morning for other three days, when the animal made its escape. Once or twice it was cheated into eating the powder when enveloped in meat, but it mostly had to be forced down the throat. The creature was altogether unaffected, and played about, was quite natural, and the pupils were rather dilated than contracted. No muscular weakness was observed.

12. To a small, smooth-haired terrier bitch four grains were given, enveloped in meat, night and morning for three days, and then five grains for other five days, when it was used for Experiment 15. No effect whatever was induced. The dog was playful and cheerful, neither purged nor sick. The pupils may be said to have been unaffected; for though at times they appeared contracted, at others they were dilated. He did not show any symptoms of paralysis or weakness. He was not thirsty, but very hungry, being kept on low diet so that he might eat the meat on which the bean was put, and also that this might have every opportunity of inducing its full effect.

13. To a small but strong rough-haired terrier, which would eat anything, four grains of the powdered bean were given night and morning for two days. On one occasion it got eight grains, as it snatched the other dog's portion from it. For other two days five grains were given night and morning. For the next two days its dose was six grains twice a day. This was then increased to eight grains for three days; and for one day three doses of eight grains each, sometimes in meat, at others mixed with gravy, were given. During all the time the dog was as vigorous and active as possible, showing no abnormal signs whatever. The pupils were unaffected.

14. To this same bitch I gave forty grains of the powdered bean, supposing it would produce a full if not fatal effect, intending to administer strychnia on decided symptoms of poisoning been shown. However, for an hour but very little effect could be perceived, when she became weak and indisposed to run about. Though she was still able to jump upon a chair, yet she could not upon a table, as she had before done. The hind legs were decidedly more affected than the fore legs. The pupils were neither contracted nor dilated. She was quite cheerful, and mentally unaffected, but disposed to sleep. The next morning the dog was weak and unsteady upon its hind limbs, but active, and not so much affected that one who did not know the activity of the dog, or who was not a close observer, would probably have noticed the change in its gait, or considered it under the influence of the bean.

The following three experiments and post-mortem examinations will show how little truth there is in some assertions which have been made as to the neutralizing effect of Calabar bean and strychnia upon each other.

15. Half a grain of strychnia was well mixed with twenty grains of finely-powdered Calabar bean. Being thoroughly enveloped in meat, they were given to a mongrel dog which weighed about twelve pounds. No effect whatever was observed for twenty minutes, when he became restless, and, in walking, was stiff and upright on the limbs. This

symptom increased, with roundness of the back, and rapid, imperfect respiration from tightness of inspiratory muscles, until twenty-seven minutes, when he had as violent and long-continued a convulsion as I ever saw, and lay as though dead; but he revived, and, though unable to rise, ate a piece of meat, and afterwards staggered a few steps with the four legs stiff and widely stretched out, when a second convulsion seized him, and forced the urine to flow. This had barely passed away, when a third convulsion came on, which, after five minutes' more or less violent duration, ended in death. During the whole period the pupils were dilated.

Autopsy, forty-eight hours after death.—Body very rigid; muscles of a full dark-red colour and firm; lungs collapsed, pink in colour, and did not contain any fluid; bronchial tubes normal; venæ cavæ enormously distended. Heart firmly contracted, particularly on the left side, which contained a little dark coagulum; the right cavities were distended with nearly fluid black blood. All the abdominal viscera were congested. The bladder contained a little urine, and the rectum was full of fæces. The brain and its membranes were excessively congested, as was the medulla spinalis and its membranes. The spinal veins were enormously distended.

These appearances are precisely those found in animals *who die while in violent convulsions*, whether they be induced by strychnia, chloroform, hydrocyanic acid, or other similar agents.

16. One-third of a grain of strychnia was carefully mixed with two-thirds of the spirit extract obtained from a Calabar bean which weighed about sixty grains, and given on meat to the dog used in Experiment 12, which had had repeated doses of Calabar bean for eight days. It was quite unaffected for half an hour, when, though cheerful and running about, the limbs became stiff, and the respiration imperfect and hurried, with frequent retching, as though from spasm of the throat, without vomiting. It was offered water, but would not drink. The back of the head was decidedly hotter than any other part of the body, and the muscles of the neck were very stiff. It appeared frightened, and desirous to seek for protection. Up to an hour it lay quietly at my feet, with all the muscles very rigid, except once, when, on some one coming to the door, it suddenly jumped up, ran to the door, and barked fiercely. It was now seized with as long and terrific a convulsion as I ever saw, which continued with only partial intermission for five minutes, when the dog was dead. The pupils were dilated all the time.

Post-mortem examination of chest immediately.—On opening the chest the lungs were greatly collapsed; they were pink in colour. No

pulsation of heart. It, like all the muscles, was perfect flaccid.* Both sides contained some blood; the right far more than the left. The venæ cavæ were much distended with black blood. Twenty-four hours afterwards the heart, as all the muscles, had become hard and rigid. The blood in its cavities had formed a soft coagulum, firmer and darker in the left ventricle than the much larger quantity in the right ventricle. The lungs had become dark from the gravitation of the blood. The trachea was clear. The brain and its membranes were engorged. The spinal marrow and its membranes, and particularly the spinal veins, were greatly congested.

17. This bitch was the same as that employed in Experiments 13 and 14, to whom twenty-four hours before, forty grains of powdered Calabar bean had been given, and who had had considerable doses for many preceding days. Though sensible and able to run about all the day, she had been decidedly weak and tottering in the limbs, so that she was as much saturated with the bean as an animal well could be with safety. I now gave to it sixty grains of the Calabar bean, which had previously been mixed with a little hot water in the expectation of obtaining the full power of it at once. The dog showed for fifty minutes little effect, when it was purged, and weaker in the limbs. At sixty minutes it could hardly stand, but staggered restlessly about, trying, as so many of the others did, to get into any corner or out-of-the-way place. As it was again purged, it was turned out into the yard; it staggered away, and being night, was lost for a few minutes. It was found in the dung-hill, where it had got, but had fallen down, and could not get back again. It was completely under the influence of the bean. Half a grain of strychnia dissolved in one drachm of water slightly acidulated with acetic acid, was now poured into the throat. In five minutes afterwards

* Flaccidity of the muscles *always* occurs, whatever the cause of death, at the moment of death, no matter how convulsively rigid they may have been immediately before, and how great the cadaveric rigidity may shortly become. This fact has not always being recognised, even by some who should have known better. For instance, on Palmer's trial it was gravely stated that one proof of a death being caused by strychnia was, that the tetanic spasms did not cease at death, but that the body is continuously rigid; whereas nothing can be more contrary to fact. No matter how large the dose of strychnia, or how ferocious the spasms, immediately after death the muscles are as flaccid as possible, and the limbs may be placed in any position whatever, and that position they will maintain when the cadaveric rigidity sets in. This rigidity is not indicative of death by strychnia, as has been asserted, but of sudden death, while the muscles have been strongly contracted and are unexhausted in their force, whatever the cause of this action may be. Infantile convulsion, epilepsy, death on the battle-field from a bayonet or sword wound, chloroform, hydrocyanic acid, and many other agents, when causing death by convulsion, will in the dead body exhibit a strong muscle contraction and as exaggerated contorted forms as strychnia ever does.

it was quite under the influence of the strychnia, with open mouth, tongue out, hurried panting respiration, with hardly any motion of the ribs. It was excessively restless, wildly staggering about with stiff limbs, and greatly distressed, with great difficulty of breathing from the spasms of the throat. Twenty grains of the bean, in one drachm of water, were now forced down its throat. At ten minutes it eagerly attempted to lap water, but could not from spasm, and it was seized with a violent convulsion, the respiratory and pharyngeal muscles being particularly affected. As this a little subsided it refused meat, but made most determined efforts to drink, in doing which a drop or two of the water passed into the trachea, and induced a mucous râle. The distress in the pharynx from the local effect of the strychnia was great. After a very partial intermission of the spasm, a most violent and long convulsion came on, and did not cease until death, at twenty-five minutes after the strychnia had been given. For the last two minutes it was insensible, and there was only an occasional throb of the heart, and a feeble inspiration. The pupils were dilated all the time.

Autopsy, twenty-four hours after death.—Muscles rigid. The brain and its membranes, the spinal cord and its membranes, and the spinal veins, were all congested, but not quite in the same excessive degree as in the two other dogs. Lungs collapsed and pink at the upper part; dark and congested at back and lower portions (from gravitation); rather crepitating. Smaller bronchial tubes contained frothy fluid; venæ cavæ full. Heart, particularly left side, firmly contracted; this contained a little blood; the right cavities much more. In the heart the blood formed a soft coagulum; in the veins it was fluid. The muscles were of a dark-red colour.

2nd. What is the best solvent for the active principle of the Calabar bean, and how may this be most conveniently used in practice?

Presuming from analogy that the active principle in this seed was an alkaloid like that in so many plants, or, if not an alkaloid, a resinous or oily matter,—and knowing that after spirit had been made to extract all it is capable of doing, yet that the mass left retains sufficient power to be actively poisonous,—I thought it not unlikely that ether or chloroform might be better solvents, and more nearly exhaust the whole of the active matter than spirits does; or that possibly an acid might succeed better. The following experiments accordingly were undertaken, with the assistance of Mr. Reynolds, of Leeds, to whom I am materially indebted for his valuable aid in conducting the processes of extraction:—

Bean weighed when finely powdered 59 grs.

Treated with cold ether for twenty-four hours, filtered, and the filtrate distilled. This was evaporated on a water bath, and yielded

·7 gr. of extractive; this was a greenish oleo-resin, staining paper from its fixed oil.

The macerate left was now treated repeatedly with boiling ether. On being similarly evaporated it yielded only ·1 gr. of extractive.

The macerate was then treated repeatedly with boiling spirit, which, on evaporation, yielded of brownish extract 3·1 grs.

Bean weighed when finely powdered 73·6 grs.; this treated with cold chloroform yielded ·5 gr. of extractive.

The macerate was treated repeatedly with hot chloroform, and yielded ·2 gr. of extractive.

A bean with a brown-coloured kernel weighed when finely powdered 70·8 grs. It was treated with boiling spirit in a retort for three hours, the spirit being returned as it condensed, and yielded on water-bath evaporation 6·0 grs. of a brown resinous extractive.

A bean with white kernel, weighing when finely powdered 62·5 grs., similarly treated with boiling spirit, yielded of brownish extractive 4·9 grs.

A bean, weighing when powdered 75·2 grs., was treated by decoction with distilled water, and yielded 34 grs. of extractive.

The macerate of this, treated with boiling proof spirit, yielded a very small portion of extractive, which, unfortunately, was not accurately weighed.

A bean, weighing when powdered 53·3 grs., was digested with boiling water, acidulated with hydrochloric acid, until all was reduced to a soft pulp; then strained, evaporated, and moderately supersaturated with slaked lime. The precipitate was collected, dried, and digested in absolute alcohol. The filtrate evaporated yielded ·3 gr. of extract or alkaloid (?), which retained a very slight trace of lime. This was dissolved in 20 grs. of glycerine, = 1 part extractive in 66 grs. of the solution.

At the result of the above experiments I was greatly surprised, and still more so at the effects of the extracts when used, as will be seen under the third query. I would here merely remark on this latter point, that all the extracts were evaporated to as near dryness as could be prudently done to obtain their weights correctly, and to drive off the whole of the solvents, lest their irritating effects upon the eye should interfere with the correctness of the result. The extracts were dissolved in glycerine, by which they may apparently be preserved for any length of time in a fit condition for use.

While cold ether only dissolved $\frac{1}{8}$ part of the bean, and boiling afterwards only extracted the $\frac{1}{60}$ part in addition, together a mere fraction beyond the $\frac{1}{4}$, boiling spirit after this extracted the $\frac{1}{5}$ part by weight of the bean. Chloroform extracted less than ether; for, by cold

chloroform, from a large bean weighing 73·6 grs., only ·5 gr., = $\frac{1}{147}$ part, was got; and, by hot chloroform, ·2 gr., = $\frac{1}{568}$; or, together, = $\frac{1}{106}$ parts by weight of the bean. By boiling spirit, from both the brown and white bean, a very much greater proportion of extract was got, being from the brown $\frac{1}{12}$, and from the white bean fully $\frac{1}{13}$ of their weight. But water dissolves a much greater proportion still; for by this process nearly one half of the entire weight of the bean is got in the form of an extract; from a bean weighing 76·2 grs., no less than 34 grs. were obtained. The proportion of extract, or alkaloid, if it be one, was very small from a bean weighing 55·3 grs.: only ·3 gr. was obtained by digestion in hydrochloric acid—not more than equal to $\frac{1}{184}$ part.

The preparations used for local application to the eye were the above dozen extracts. A preparation of Mr. Squire, of Oxford-street, London, being a paper saturated with a tincture of the bean; a similar paper prepared by Messrs. Bell and Co., of London; a tincture made by Mr. Squire, to whom I am indebted for a liberal supply of both paper and tincture; and a preparation in capillary tubes made by Messrs. Bell and Co., which is, I believe, a solution of the spirit extract in glycerine, so placed to secure its preservation. The watery infusion, though possessing some activity, is, from its bulk, muddiness, and quick decomposition, an inconvenient preparation, not likely to be much employed.

3rd. What is the effect upon the eye when locally applied? From the statements which have already appeared from several observers, almost everybody now knows that the effect is to contract the pupil, so that it would be useless to repeat in detail the numerous experiments which I have made upon the eyes of different animals; but some must be given to illustrate the effect of the different preparations, so that the deductions may be understood, and the physiological importance of others shown.

Ether extract.—Powder first treated by cold, afterwards by hot ether; both extracts dissolved in glycerine.

Old terrier dog. Into the right eye the cold extract was put; into the left the hot extract. Considerable irritation, redness, and lachrymation were instantly induced in both eyes, but the most in the left. In five minutes both pupils were somewhat contracted, the right most so, but in neither was the effect great, and in twenty minutes had passed away.

Skye bitch. The hot extract was put into one eye, and the cold into the other eye. Redness, lachrymation, and irritation were as before caused, which, however, soon passed off. No effect whatever was produced upon the pupils.

Two days afterwards the experiment was repeated with the same result.

Upon a full-grown cat a similar experiment was performed. Considerable, but temporary, irritation and watering were induced; the pupils were rather dilated than contracted.

Upon a half-grown kitten a like application was made with like results, except that the left pupil, where the cold extract had been applied, was decidedly dilated.

Into the eyes of two men and a boy both the hot and cold extract were put several times, without any contraction of the pupils being caused. Redness, irritation, a little pain, and lachrymation were always at once induced for a few minutes.

Chloroform extract.—Powder treated first by cold, afterwards by hot chloroform; both extracts dissolved in glycerine.

Upon the same two dogs, two cats, two men, and boy, similar and repeated experiments were made; the cold extract being put into one, the hot extract into the other eye. Some smarting, considerable irritation and redness, with free lachrymation, were for a short time induced. In one experiment the cold extract produced some slight temporary contraction of the pupil, with which exception no effect upon the iris was observed.

Water extract.—First treated with repeated boilings of distilled water, residuum afterwards with boiling proof spirit. The extract obtained by water, when put into the eyes of cats and dogs, produced very little irritation or redness, and very little effect upon the iris; perhaps some contraction was caused, but it was very slight in comparison with the effect of the pure spirit extract. The effect of the residuum treated with boiling proof spirit was greater than the simple water extract, but not so great as that obtained from the bean by alcohol; though, as I am not sure that in the evaporation of these extracts somewhat too much heat was not used, I would speak of the effect of them with more reserve than of the other preparations.

Hydrochloric acid extract, dissolved in glycerine. This I tried by introducing it into both eyes of two dogs and two cats. In one of the dogs it instantly caused great irritation, redness, and watering; I think, also, much pain, which continued for some considerable time. In the other dog, though present, these symptoms were in a much less degree, and in the two cats in a still less, though they did not appear to be very comfortable. The effect upon the pupils was not considerable. In the first dog no contraction was induced, the extract probably being washed away by the lachrymation. In the other dog and the cats the contraction of the pupil was slowly developed and by no means great, but it continued most of the day. The experiments were made early in the morning. By evening all contraction of the pupil had disappeared, though the dog's eyes continued red and irritable even on the following morning.

Spirit extract. Three kinds of extract; first, that obtained after cold and hot ether, had extracted what they would dissolve; second, that obtained by boiling spirit from a brown kernel bean; and third, that from an ordinary white bean. All dissolved in glycerine. Numerous experiments have been made upon dogs, cats, men, and boys with these three extracts, of various strengths, ranging from one grain of the extract in twenty of glycerine, to one grain in sixty of glycerine. In all the effect has been contraction of the pupil. In the great majority of cases neither pain nor redness, and but little watering have been caused. In some few cases, however, there was pain and considerable lachrymation when, from, I presume, the preparation being washed out, the effect was slower and more imperfect. In most cases the effect is seen in less than five minutes, and in some in less than thirty seconds contraction may be observed beginning. Within an hour the full effect is almost invariably established. In from four to six hours the intensity usually lessens, within twelve hours it has greatly abated, and in twenty-four, so far as I have observed, it has altogether disappeared. In the three extracts I observed very little difference in the effects produced: that obtained by spirit, after ether exhaustion seemed to possess nearly, if not quite as much, power as either of the others.

Bell's glycerine extract, in capillary tubes. Half the contents of a tube was blown into each eye of a Scotch terrier bitch. No irritation was induced. For ten minutes no effect was perceived, when both pupils began slowly to contract, and continued to do so for seven or eight minutes, until considerable but not excessive contraction was established, particularly in the right eye. They continued in the same condition for two hours; in four the effect was subsiding. Neither gas-light nor candle light placed close to the eyes had any influence. The next morning the effect was subsiding, though the right was still the smaller pupil. In twenty-four hours both pupils were natural.

An African bitch, a most timid and excitable creature, had the extract blown into the right eye only. Contraction of the pupil *instantly* began; in two minutes it was not half the size of the left, and in ten it was not a quarter the size. The pupils continued in this state for half an hour, the left being widely dilated, while the right was not a fourth of its size. A lighted candle was now placed before the eyes, by which the dog was greatly alarmed, and struggled hard, when the left pupil contracted and the right dilated, so that for a time they became equal in size; but so soon as the candle was removed, and the dog became calmer, the former inequality returned. At four hours the contraction of the right iris had passed away, and both pupils had become widely dilated. No contraction in either pupil could be induced by either gas or candle light. The following morning both pupils were alike and normal.

Paper saturated with tincture of Calabar bean, as prepared by Mr. Squire and Messrs. Bell and Co. By far the greater number of experiments made with Calabar paper have been with that sent to me by Mr. Squire. The animals upon which these have been tried are several dogs, many cats, four horses, one pig, four cows, six sheep, four fowls, and a great many human subjects. These, with the exception of the sheep, which I shall have to refer to, I need not particularize. The effect upon all animals is uniform: contraction of the pupils, pretty much, I think, in proportion to the size of the piece of paper inserted, and the retention of it for a time in the eye. This latter point is one of importance, and if not carefully noted may lead to error. In some animals it will remain for thirty-six hours or more quietly enough; but in others, either from the lachrymation excited, it is speedily washed out, or, from the irritation its mere presence as a foreign body excites, it is soon got rid of, and hence its influence lost; I say for a time, for, so far as I can judge, if retained for two hours, or even less, the effect is as great as if retained for twenty-four, the influence being exhausted in this time.

Of all animals cats are the best for experiment, their active and brilliant-coloured irides showing the effect most markedly. In horses, oxen, and sheep, the effect is not so great. In them the iris is not naturally so active and mobile; hence, I presume, the less effect upon these oval-pupiled animals than upon the more actively moving pupils; and a much longer time is required, particularly in oxen, for the full effect to be produced, whether Calabar or atropine paper be used. In some eyes, where in two hours I thought very little effect would be caused, in twenty-four hours I found full effect had occurred; and in one cow, where I had put atropine paper into one eye and Calabar bean paper into the other, while there was very little result in two hours, in thirty-six I found the one pupil widely dilated and the other closely contracted, more so than I have seen in any other ruminant.

I have been wishful to try the effect upon the more actively moving pupiled birds—as parrots, owls, and hawks; but hitherto I have failed in obtaining subjects for experiment. In the common fowls I have been disappointed in the result; for though I have used both Bell's and Squire's paper, and also Squire's tincture, in both eyes of the same fowl, and also in one eye, while I have put atropine paper into the other, I have seen comparatively little effect. It is very difficult to keep the paper in—a free secretion of fluid is poured out, and the birds are in great excitement; which may in part, if not wholly, account for this.

A lamb. Squire's paper was put into the right eye: in a short time (less than half an hour) the pupil contracted, and continued fully half contracted up to seven hours, when the lamb was killed, the left pupil being unaffected.

A lamb. Calabar paper was put into the right eye, and atropine paper into the left. The right pupil became greatly contracted, the left greatly dilated, and so continued for seven hours, when the animal was killed.

A lamb. Similar experiment as the last, with precisely similar effect.

An old sheep. Similar experiment—the Calabar paper in one eye and atropine paper in the other—with precisely like results to the last two. The effect was intense: the left pupil (atropine) was greatly dilated, the right pupil (Calabar) greatly contracted.

A sheep. Calabar paper put into both eyes: in three hours both pupils were rather but not much contracted; in seven hours the right pupil was rather more contracted, but the left pupil was not. Calabar paper was again put into both eyes: the next morning—twenty-four hours after the first putting in, and seventeen after the second—the paper was still in the left eye, not in the right. Both pupils were alike, and unaffected.

A sheep. Calabar paper put into the right eye only: in three hours, the paper being still in, the pupil was considerably contracted; the left eye unaffected. Killed.

A sheep. Both Calabar and atropine papers were put into the eyes: in three hours both papers were in the left eye, the atropine only in the right eye, but *both* pupils were alike somewhat dilated: in six hours the pupils were in the same condition, the papers being still in as at three hours. Now (at six hours) both Calabar and atropine papers were again put into both eyes: the following morning, twenty-four hours after first putting in, both papers had disappeared from the right eye; in the left the Calabar paper was still present, but not the atropine. Both pupils were alike, and unaffected.

Tincture of the bean.—This, as prepared by Mr. Squire, is of pale-brown colour, not unlike pale brandy. Though not strong nor unpleasant to the taste, it yet, when placed upon the tongue (to me), leaves a rather pungent feeling at the spot, and induces a sudden sinking feeling of nausea at the stomach. It acts readily and well, producing almost instantaneous contraction of the pupil. It is too strong to use alone; indeed, the spirit it contains would preclude its employment undiluted, but when mixed with water it is readily borne, and is effective. I have tried it on many animals and scores of human subjects with the uniform effect of contracting the pupil. I added two drops of the tincture to twenty of water, and put it into the eyes of five persons who were suffering from slight diseases of the appendages of the eye, the globes being unaffected. In all full contraction of the pupil was within an hour fully induced, without causing pain or any unpleasant feeling.

Continued contraction of pupils.—I have stated that in twelve hours the effect has considerably subsided, and, in twenty-four hours, commonly entirely passed away. Hence, if permanent contraction of the pupil be desired, repetition of the application is necessary. In cats and dogs, by the daily repetition of the local application, I have kept the pupils in a state of contraction for a week: in one man for ten days, in another for a fortnight, and in a boy for nearly one month. In twenty-four hours the effect had in all cases nearly, if not altogether, subsided. I used for this purpose the various preparations before named. The chloroform, ether, and aqueous extracts I repeatedly tried, and always, particularly the first two, found that they failed; the others, which had been extracted by spirit, always succeeded. The effect appeared not to vary from day to day. No inconvenience was caused; and, on the cessation of the application, the effect passed off.

When atropine is put into one eye, and Calabar bean in the other, they act quite independently of each other, neither in any way being influenced by the other. When placed in the same eye together, or one after the other, they are antagonistic to each other; and though in several experiments which I have performed, where I have placed the two together in the same eye, or more frequently where, after the pupils have been dilated by atropine, Calabar bean has been introduced shortly afterwards, I have seldom succeeded in observing that the effect of the one counterbalanced that of the other; and, indeed, have doubted, after the pupil has been *fully* dilated by atropine, if the Calabar bean exercised any very great effect in contracting it, it is possible that this only arises from the strength of the two not having been adjusted; and that if this problem were correctly solved, the two might be found to neutralize each other.

As Dr. Christison has well remarked in his description of this bean and its effects upon himself, it is by no means so easy, as those who are not accustomed to delicate physiological investigations, might suppose it to be, to accurately determine the precise *modus operandi* of many poisons, particularly when death quickly ensues. Hence numerous errors have prevailed, and probably even now some exist, as to the true action of many poisons with which we have long being acquainted, and with which experiments have frequently been made. To no poison is this remark more applicable than to the Calabar bean. In addition to its speedy depressing action, in which motive power is lost, all means of expressing sensation or intelligence are soon impaired and destroyed, so that it becomes extremely difficult to feel sure whether the non-expression arises from non-perception, or the loss of the capacity of indicating what is perceived; and as after death literally no abnormal changes are found in any of the organs or

tissues, the more reliable indications of the parts primarily acted upon by the poison are wanting. We are thus reduced to inferences drawn from the observance of phenomena exhibited during life, which are very liable to be misinterpreted. Dr. Harley, I see from a paper recently published,* considers that life is destroyed by the drug "paralyzing the nerves which supply the respiratory muscles—being, in fact, a respiratory poison;" but I rather incline to agree with Dr. Christison in the supposition that death results from paralysis of the heart. Not that I believe the bean acts specifically upon the heart, but that the contractile power of it, in common with that of all the other muscles, is suspended, and hence that no blood is circulated. Of course, as respiration is most feebly and imperfectly performed, the failure of this function will also assist. That this is the effect when the dose is large and death speedily ensues, I feel little doubt. Were death caused by suspended respiration, the appearance of the lungs and heart would resemble that found after death by asphyxia. The lungs, and heart, particularly its right side, would be found gorged with black blood. This, however, is not the case, for the lungs are found pale and, on opening the chest, greatly collapse; while the right side of the heart is not greatly distended, the blood is not dark, and there is a difference of colour on the right and left sides of the heart. It is, however, very probable that a considerable difference in the mode of death and the post-mortem appearances will be found, according as the dose is large, and death speedy, or the dose smaller and death slower. In the latter case, as the respiration is more and more imperfectly performed, while a feeble stream of imperfectly oxygenated blood is passed through the body, the later symptoms during life, and the appearances after death, will approach more closely to those resulting from pure asphyxia.

But whether death results from suspension of the contractile power of the heart (syncope), or of that of the respiratory muscles (asphyxia), it is questionable whether either should be regarded as more than a secondary cause. What induces this powerlessness of these muscles? Is it owing to some direct action upon them or either of them, or to the loss of the nervous influence by which they act? and if the latter, upon what part of the nervous system is the effect produced? Dr. Fraser, to whom, after Dr. Christison, the profession is most indebted for calling attention to this bean, considers it is the spinal cord which is primarily affected, and that the Calabar bean is a direct depressor of the cord,†

* British Medical Journal, for Sept. 5th, 1863.

† I regret that I had not the opportunity of reading Dr. Fraser's excellent and elaborate dissertation on the Calabar bean until after most of my experiments were made, and the inferences drawn from them publicly announced. The dissertation will be found in the *Edinburgh Medical Journal* for July, August, and September, 1863.

acting more especially upon the motor columns, and hence the muscular paralysis. This may be the case; but I am not so certain that it is, and I should require further investigation before I considered the question to be proved. Though much has been done during the last few years to explain and analyze the functions of the different portions of the nervous masses and the cords in connexion with them, I am by no means certain that we can consider their respective functions to be so clearly and unequivocally separated and determined as some appear to be; nor that we are altogether in a position to speak, as is now often done, of one agent being a depressor, and another an excitor (using the ordinary meaning of the words) of the respective portions of the nervous masses. Calabar bean has been declared to be a depressor of the spinal cord, strychnia an excitor of it, and that, as their actions are contrary, the two will neutralize and destroy the effects of each other. But is this demonstrated?—is it absolutely true that paralysis of the muscles is always synonymous with depression of the spinal cord, and over, irregular action of the muscles with excitement of it? The idea is plausible, and supported by many facts, physiological and pathological. But I pause and wait for more evidence before I can admit as undeniably true the broad statements made, as to the action of agents such as those under consideration. That the action of the bean is not upon the cerebrum is most probable. All the senses appear altogether unaffected, and so does volition; but it does not necessarily follow that the effect must primarily be upon the spinal cord, and be a suspension of its motive power. The effect may be upon the ganglionic system of nerves quite as much as upon the spinal marrow for anything that I see to the contrary; or, so far as is known, it might even be upon the muscular tissue itself, rendering it incapable of obeying the nervous influence. The evidence as to the muscles contracting for some time after death, and the sequence in the order of the cessation of the contraction of the four cavities of the heart, is really of no weight whatever, as those who will destroy animals by many other agents or means, and carefully watch them, will admit. Give hydrocyanic acid, chloroform, and many other anæsthetics; remove the cerebral mass, pith the animal, or entirely remove the spinal marrow, and the same will be seen to be the usual order of things. No more organic change after death is to be found in the spinal cord, than there is in the muscles.

One argument which has been relied upon—the contraction of the iris—to show that the functions of the upper part of the spinal cord, from which the nervous fibrillæ which govern its dilating power are now supposed to arise, are depressed, would rather, I think, tend to prove, not that the spinal cord is the part primarily influenced, but the sympathetic nerves, of which these fibrillæ are a part. This is a view, which the

feeling of excessive sinking at the pit of the stomach, with faintness and nausea, so speedily induced by eating a little of the bean, would also countenance. Everybody knows what intense depression of the entire muscular system is induced by impressions made upon the solar and cardiac plexuses, even to sudden death from prostration, from an apparently trivial cause. Besides, I can hardly conceive it to be possible that such intense contraction of the fibres of the iris, which certainly results from an active motive power, such as would imply a stimulus, is consistent with a total depression of the cord. If the action of the poison were exclusively upon the spinal cord, we should find that, when the whole system is, so to speak, saturated with it, from its absorption into the blood, and when a much more considerable quantity of it must be carried to the whole cord, as when it is administered internally in large and repeated doses, that the contraction of the pupil would be much more decided and long-continued, if this arose from paralysis of the fibrillæ going to it from the cervical spinal cord, than when the agent is only in minute quantity applied locally to the eye. Whereas the contrary is the case. In fact, while contraction of the pupil in the local application of the agent is the striking fact, in the internal administration this contraction is hardly perceptible; often it is not seen at all, and never is observed in an extreme degree.

I make these observations, not as asserting that the action of the bean is specifically and primarily upon the muscles or sympathetic nerve, but to guard against it being too hastily assumed as proved that it is upon the spinal cord, and as a depressor of it. A false fact taken as a true one has often done, and in physiology and pathology I fear still does, more harm than many false theories.

How far the idea is correct that Calabar bean and strychnia are antagonistic to each other, or rather, how far the action of the one neutralizes and destroys that of the other, Experiments 15, 16, and 17 will show. From them we can hardly think the notion that the one may be used as an antidote to the other with much prospect of success, will be found to be true. The suggestion is founded upon the one being an excitor, the other a depressor, of the spinal cord, and that the two actions will destroy each other, as an acid and an alkali do. So far as I can judge, the effect of the strychnia was as speedy and as violent as if no Calabar bean had been administered. It is true that it is possible the quantities of the two substances were not correctly adjusted to procure the desired neutralizing effect; but I think it will hardly be asserted that the system could be brought more under the influence of the bean, so as to give it fuller play, or that a larger quantity could be given with any chance of success, than was done with at least two of the dogs; and yet the tetanic

spasms during life, and the post-mortem appearances, were those of uncontrolled strychnia action.

I would, by way of parenthesis, and as intimately connected with this inquiry, observe, that in my judgment the received opinion as to the cause of death by spasm of the respiratory muscles in strychnia poisoning is not, as a rule, founded in fact. I believe death more generally results from the heart, similarly to the other muscles, being involved in tetanic spasm; that the strong left ventricle is completely closed, and does not admit any blood into it, so that none is circulated through the arteries, whereby it is forced to accumulate in the lungs, right side of the heart, and large veins. This happens in all cases where the spasm is great and continuous, and the animal dies while strongly convulsed. In such, I believe, the left ventricle will always be found firmly contracted and empty, and the right ventricle and auricle engorged with fluid, or nearly fluid, dark blood. To observe this the chest should be carefully opened, without wounding the large veins, before the head is touched; for if the head be first opened, the fluid blood will drain away from the cut sinuses, when the heart will be found empty, and hence supposed not to have contained blood, whereas on the right side it has been engorged. But if the dose of strychnia has been barely sufficient to destroy life, so that this has been prolonged, and the spasms have ceased for some time before death, then, as the respiratory function has been most imperfectly performed, the post-mortem appearances will more nearly approach those of asphyxia: the left side of the heart will not be so firmly contracted, but will contain dark blood. In some cases it is quite possible that, as in true tetanus, the animal may be simply asphyxiated, by spasm of the glottis. In the first case, where the animal dies in spasm, the cerebral and spinal veins will be greatly engorged; in the latter they will be found but little distended: for it is the violent and long-continued spasm of the muscles which forces the blood into these large veins, where there is no counterpressure from the atmosphere to resist their distension, and not, in my judgment, any specific action of the strychnia. I have often seen precisely the same conditions after poisoning with aldehyde, hydrocyanic acid, conia, narcotin, and other substances, according as death occurred during the continuance of the convulsion, or not, until they had for some time ceased.

Before leaving this subject it is of importance and interest to call attention to the curious and remarkable fact, that by putting Calabar bean into one eye, and atropia in the other, we may have the one pupil shut up so as to be barely visible, the iris appearing almost entire, and the other pupil so greatly dilated that the iris has almost ceased to be visible. This fact is of great importance in illustrating the action of agents upon

the animal economy, and, in my opinion, proves that at least some of them have a local effect independent of their general action. Some good and well known modern physiologists have contended that all poisons and other agents act only when absorbed, and are carried to the central nervous masses; that they do not act primarily upon the terminating nervous fibres, but only upon the centres, and secondarily upon the extremities. The fact which many years ago I demonstrated, that by the local application of chloroform and several other anæsthetics we can so completely destroy the sensation of portions of our own bodies, and even of the entire extremities in the higher animals, as in the cat and rabbit, that a limb may be amputated, the creature being perfectly indifferent to and unconscious of the operation, retaining all the time the full possession of its faculties, and having full power over its other limbs, satisfied me that, though substances when swallowed do act generally by absorption into the blood, yet that they also act upon the particular nerves to which they are applied, quite independently of the central masses. This, however, has not appeared so conclusive to some inquirers as to myself. In what way it can be explained that by one agent we may shut up one pupil, and at the same moment by another agent enormously dilate the other pupil, otherwise than on the supposition of their local action, I know not. Were it by a general action upon the central nervous masses, though a reflex one, if any effect were caused it would be of a negative kind. We cannot have one pupil shut and another opened by two dissimilar forces acting generally; even were this possible, the effect would be varied. It would not always be the same eye which was alike affected; whereas it is invariably that into which the bean is put which shows a contracted pupil, and that into which the atropia is put which shows a dilated one. How otherwise than as independent and local effects these two dissimilar actions can be exhibited at the same moment I cannot conceive. Moreover, when the bean and atropia are together put into the same eye, either no effect whatever is produced, or only so partial a one as to show that they neutralize each other. This also must be a local action.

It has been stated by some observers, and truly so, that when the extract of Calabar bean is put into an eye, the pupil of which is preternaturally dilated, contraction of it will follow. Now mydriasis is commonly caused by disease of the cerebrum affecting the origin or the trunk of the third pair of nerves, or some pressure external to the skull upon its branches, which paralyzes the action of the filaments which go to the iris, unless from traumatic injury to the eyeball itself. It is difficult to account for the contraction of the iris taking place under such circumstances on the supposition of the agent acting exclusively upon the spinal

eord; if it does so, obviously it cannot influence the functions of the cerebral nerves. Contraction in such a case cannot be caused by stimulation of the nerves going to it. The contraction could only result from paralysis of the sympathetic or dilating nerve destroying an active dilating power, and so permitting what may be supposed to be the natural elastic physical forces of the iris tissues to counterbalance each other. This most probably would be the explanation offered by those who adopt the theory of spinal depression. As, however, in this case the agent is applied locally, and, so far as symptoms indicate, acts locally alone, supposing that the idea of the contraction of the iris depending upon paralysis of the dilating power is true, it would, I imagine, rather be an argument for the opinion that the agent acts generally upon the sympathetic nerve in all the symptoms induced than upon the spinal cord exclusively, and, *pro tanto*, militate against the theory of spinal depression.

Contraction of the pupil, it would appear, may be induced by the application of the bean, in almost any form of mydriasis, whatever be its cause, provided the texture of the iris be not destroyed, even though the iris be altogether insensible to the action of light. In a middle-aged woman suffering from some deep-seated cerebral disease, but otherwise healthy, and who has in consequence had two epileptic seizures; in a man with more general brain-affection, causing paralysis and numbness of all the extremities, and considerable difficulty in articulation; in an old man who lost one eye many years ago, and more lately the other from disease of the choroid and deposit upon the retina; in a fourth, with dilated pupil from a large incised wound cutting through the cornea, and extensively dividing the iris; in a fifth where there was intense dilation of the iris and amaurosis from a blow upon the globe, which had been followed by disorganisation of the retina, and in a sixth case of amaurosis from an apoplectic clot upon the retina, I have got full contraction of the pupil by the extract of the bean.

It has been asserted by Dr. Robertson, Dr. Harley, and others, that the action of the bean, when applied to the eye, is that of a stimulant to the ciliary nerves, thus inducing contraction of the ciliary muscle, and rendering the eye myopic. This statement may at the first blush appear plausible to some; but I confess that it seems to me to be an unfounded supposition, resting upon, to say the least, an unproved hypothesis as to the functions of the ciliary muscle. It is perfectly true that, *cæteris paribus*, the pupil is commonly contracted when near objects are looked at, and more dilated when distant objects are regarded. This, however, is only one of a series of effects which take place in the eyeball, and probably is rather an optical than a physiological change. The smaller

aperture in the diaphragm is merely to exclude the more oblique rays, which cannot be brought to a focus upon the retina, and to shut out the super-abundant light. This part of the correction of the aberration of parallax may be obtained by an artificial diaphragm with a small aperture in it held *before* the eye, the structures of the eye remaining unaltered, as any one may satisfy himself by looking at a near object through a small opening in a card held near to the eye.

I know of no one anatomical or physiological reason for the supposition that the ciliary muscle can assist in contracting the pupil, nor can I conceive how it can act on the cornea or the lens. If it have any action whatever upon the iris—which is doubtful—it is more likely to be antagonistic than adjuvant to the contractile fibres of the iris. The iris and the ciliary muscle have both a fixed attachment to the sclero-corneal junction—the iris passing directly inwards, the ciliary muscle outwards and backwards. Hence, admitting that both are contractile tissues, they may act in opposition to each other, but not, I think, in conjunction. If the pupil is contracted, the ciliary muscle will, I apprehend, be relaxed. If the straight fibres of the iris act, and the pupil is dilated, the ciliary muscle (on the supposition of assisting action) may contract; but as the pupil is contracted in near vision, I do not see how it is possible that the lens can at the same moment be pulled forwards by the contraction of the ciliary muscle. Nor can I imagine, granting the ciliary circle to be really a contractile structure, obeying the sympathetic nerve fibrillæ, how it can possibly lengthen the axis of the eye, and render it myopic. Muscles can contract only to a certain proportion of their length, and, like all other moving forces, must pull the movable attachment towards their fixed one. Now, as this fixed point is the junction of the iris, cornea, and sclerotic, and as the ciliary muscle passes outwards and backwards to be spread over the anterior edge of the choroid, its action will not be upon the firm dense ring (the most unyielding part of the eyeball) to which it is anteriorly attached, but upon the soft elastic choroid; and how its very short fibres can contract sufficiently to exert any motive influence upon the lens, vitreous humour, or retina, to none of which they are attached, I am at a loss to conceive. These parts could only be indirectly acted upon by the compression of the choroid, which more or less completely encircles them; and as this is soft and yielding, it appears to me, even allowing the full contractile power to the ciliary muscle which other muscles possess in proportion to the length of their fibres, utterly impossible that it can exert the influence attributed to it. The choroid may yield, but it will not pull the lens forward, alter its curve or density, increase the convexity of the cornea, lengthen the antero posterior axis of the vitreous humour, nor move the retina backwards—one or more of which changes must occur in the correction of the aberration of parallax.

Moreover, it appears very like a contradiction to assert that an agent may act as a depressor of the functions of the spinal cord, and, at the same moment, as an excitor of those of the ciliary or other muscles; surely one or other of these opinions must be wrong. If the argument, drawn from the weaker power of the muscles generally, that the action of the bean is a depressor of the power of the spinal cord be worth anything it must be equally applicable to the nervous supply for the ciliary muscle, whatever be the source of it; the one cannot be depressed, the other excited.

As to the argument of the active contraction of the ciliary muscle in near vision, which rests upon the sensation of fatigue when very near objects are closely examined, I do not regard it as proving anything in support of the assumption, inasmuch as an equal sensation of fatigue is perceived when very distant objects are closely watched for some time by eyes unaccustomed to such work.

Vomiting and purging are said to be commonly induced by the internal administration of the bean, but according to my experience, the bean can hardly be considered as either an emetic or purgative. Often neither vomiting nor purging occurs at all, and when they do, it is rather nausea and retching than vomiting. Sometimes a good deal of frothy phlegm will, after considerable effort, be brought up, but violent emptying of the stomach is rare. When the bean is fairly enveloped in meat or other food, so that it is not brought in contact with the buccal and pharyngeal surfaces, retching is not a prominent symptom, and vomiting by no means a constant one. Neither does salivation then occur. So with purging; there is not uncommonly a frequent straining for stool, but only a nodule of fæces or some mucus passes. It is rather mild tenesmus than violent purgation. I have never seen excessive cathartic action caused by the bean, and after death, if the animal has not been starved, the intestines—even the rectum—are found full of fæces.

I can easily imagine, from what I have observed of its effects, that these, when it is administered by those whom practice has made familiar with its management, may be materially modified. By care in the previous preparation of the individual, by the kind and quantity of food in his stomach at the time the dose is given, the vehicle in which it is administered, the quantity swallowed, the treatment to which the bean has, before employment, been subjected to, (immersion in water, exposure to heat, &c.) and other circumstances which experience would easily enable anyone to learn, considerable control may doubtless be obtained over the result. Hence, I suspect, the priests of Old Calabar, who are the officiating men in the public ordeal when the bean is judicially administered, have great power in their hands, and, in accordance with their desire, can deter-

mine with considerable probability whether the poison shall be fatal or be thrown off by vomiting and purging. Given to animals when the stomach is full, it is more likely to induce free vomiting and be thrown off, though the nausea may be less than when the stomach is empty.

The total absence of any appearance of irritation in the stomach and intestines after death is remarkable, and appears to be uniform.

Experiments 11, 12, and 13, will show that repeated doses are borne with comparative impunity, and that the poison is not accumulative; for a quantity may be given, in divided doses, with very little, if any, effect, which if given in a single dose would be speedily fatal.

Upon the second question, as to what is the best solvent for the active principle of the bean, there is little occasion to dwell, as the experiments themselves will explain all that need be said. It has formed no part of my object, as I stated at the outset, to separate this principle for analysis. That it is very difficult of isolation, as Dr. Christison has stated, is abundantly evident. With the results obtained by ether, ehloroform, and hydrochloric acid I am disappointed. Not only is the quantity taken up by them from the mass of the bean much less than is done by spirit, but the little obtained by them is very much less active and more irritating; and after they have exhausted all they are capable of doing, spirit will still extract a larger portion of more active matter than either of them has been able to do. Though water extracts a very much greater weight than spirit does, this possesses much less power than the spirit extract, and is much sooner decomposed. Hot spirit, then, as stated by Dr. Christison, is unquestionably the best menstruum for dissolving the active principle from the mass of matter. But as even this by no means extracts the whole of the active principle, it shows how tenaciously it is held in combination with the albuminous and starchy matter of which the bean is mainly composed; for the macerate left is still an active poison, as Experiment 4 shows, where twenty grains of the mass left after cold and hot ether and boiling spirit had extracted all that they would take up, produced considerable effect upon a dog.

I would by no means assert that the whole of the active principle cannot by any amount of treatment with spirit be extracted, but merely that it is retained by the mass with greater tenacity than by most other vegetable substances.

It is most important that the poisonous principle should not only be isolated, but that some certain test for its presence should be discovered; for now that public attention has been so freely called to the bean, there is little doubt that his majesty of Old Calabar will be sensible to the claims of gold, and part with the seed in sufficient abundance to more than supply the wants of civilized people for legitimated purposes, and

leave enough for those who are disposed to share with him the power of using it, if not as an ordeal, at least as a poison. I have lately been told, on what I believe to be good authority, that one chemist alone in London has sent out an order for half a ton of the beans, which is far more than, in the present state of our knowledge of its use, the whole world is likely to want for purely scientific purposes for some time to come.

Considering the absence, after a dose of the bean has been taken, of any very prominent symptoms during life, or at least of such as would be likely to fix the attention of non-medical observers; the total absence of any organic change, or even of severe functional derangement in any of the organs or tissues; the difficulty of eliminating the active principle, and the want of a test for its presence, it is most desirable that the bean itself should not be too widely distributed or made too easy of attainment, or we may expect it will be substituted for other agents, which do not promise the same immunity in their surreptitious use.

It has been stated by Dr. Harley, on theoretical grounds, and by Dr. Fraser, from the actual administration of it in several cases in which he thinks good effects have followed its employment, that the bean will become a valuable therapeutical agent in the treatment of disease where pain and vascular excitement exist. They appear to suppose that pain may be allayed by it instead of by opiates, and that vascular excitement may be calmed by it without the employment of direct depletants. I have not had experience in its effects upon the system when administered internally as a medicine. Should the favourable anticipations be proved by experience to be well founded, a valuable drug doubtless has been added to our Pharmacopœia. But knowing how easy it is to mistake the *post hoc* for the *propter hoc*, and how many sanguine hopes as to the value of new remedies have been doomed to forgetfulness by larger experience, I prefer to wait for this before expressing a decided opinion upon the value of it as an internal medicine in general disorders. I am not, however, so sanguine in the expectation of its being proved to possess superior virtues, in the control of cerebral and cardiac excitement, to other drugs with which use has made us more familiar, as these gentlemen are. That it may be safely administered I doubt not. Its deadly power is no argument against its employment. We daily use with confidence and success many remedies which possess at least equally poisonous properties, and should this one be found to be effective and constant in its action, doubtless it will soon be largely used. I have less hesitation in regard to these points than as respects the former. As an external remedy in the treatment of rheumatic and neuralgic affections, it may not improbably be beneficial. The tincture, applied by means of a camel-hair pencil two or three times

a day, or added to a soap liniment and used over the painful part, are worth the trial; or possibly an infusion used as a lotion might be beneficial.

As to the energetic local action of Calabar bean upon the pupil there is not the smallest room for doubt. There is no other substance known which possesses anything like the power it does in painlessly, quickly, and without irritation, contracting the pupil. In all cases where the pupil is preternaturally dilated, and it is thought to be desirable to contract it, preparations of the Calabar bean may be employed without hesitation.

The number of diseases in which it is desirable to contract the pupil is perhaps not very large; and, so far as occurs to my mind just now, the number in which this drug is likely to be used for this purpose is not very numerous. That dilated condition of the pupil which is the result of the application of atropia, and which is the one hitherto most spoken about in connexion with the use of the bean, I hardly regard as a pathological state; and were the use of the bean to be confined to the counterbalancing it, though at times convenient and advantageous, its value would be reduced to little more than that of physiological plaything. The dilation commonly subsides of itself in twenty-four hours; and though occasionally more prolonged, yet it is not often productive of much inconvenience after this period, and within three days it disappears. Besides, I am not quite satisfied—more particularly if there be any abnormal condition of the internal structures of the eye (and unless there be such the employment of atropia is not often necessary)—how far it is well to set up two diametrically opposing actions in the structure of the iris,—that is, forcibly to dilate with atropia, and as, or even more, forcibly to contract with Calabar bean. I incline to think it better to let the action of the atropia spontaneously subside, than to rudely destroy it, unless it should continue beyond the first day, when the introduction of the bean into the eye will be found very quickly and pleasantly to restore the adjustment of the eye to its natural condition. In certain cases of mydriasis—whether dependent upon disease in the brain, pressure upon or disease of the third nerve, or as the sequent of traumatic injury to the eyeball itself—preparations of the bean may sometimes be useful to contract the pupil, when such is found to improve near vision, or to help the focal adjustment of the eye. It must however be remembered that this will not be more than palliative. In removing a troublesome symptom it may occasionally be useful; but for the cure of the affection upon which the dilation depends, other treatment, as is now employed, must be adopted.

It is in contracting the pupil so as to withdraw a prolapsed iris

which has escaped through a wound in the cornea that I consider the great value of the bean consists. I pointed out this use in a paper inserted in *THE LANCET* for July 18th, 1863, where I related two cases in which I had so employed it. Since then I have used it in many similar cases with considerable advantage. I believe it here promises to be of the greatest value, and that it will enable us to save as useful organs, many eyes which otherwise would be altogether lost, or comparatively useless, and in a great number of cases to convert what hitherto has been a prolonged, painful, and very troublesome affection, into a much more manageable and shorter one. So also it occurs to me that in all probability, it may be valuable in those most annoying cases where after extraction of the lens the iris prolapses, and will not remain out of the lips of the corneal wound. There are few ophthalmic surgeons who have not occasionally had the mortification, after a most successful extraction, of finding the iris has prolapsed, and uncontrollable destructive inflammation has followed. Very recently, as I was operating upon an excitable woman, so soon as the knife had well penetrated the cornea, she jumped up, and could not be restrained. The knife had to be withdrawn, on which the iris prolapsed. I thought this a good opportunity of trying the effects of the bean. A portion of Squire's paper was immediately introduced under the lid, and the woman placed in bed. On the day following the wound had healed, the pupil being as round and the iris as natural as it ever was.

In granular and irritable lids; in strumous ophthalmia, where there is much photophobia; in some of the active inflammatory affections of the conjunctiva, where there is much pain and excitement, and where the contractile effect upon the iris will not be objectionable; possibly also in pure and uncomplicated retinitis, where contraction of the pupil by the exclusion of light would be useful,—a lotion of the extract of the bean may be valuable. So soon as I can obtain a sufficient supply of the bean to test it on a large scale, I shall put it to the proof in these and similar affections.

During the time, and since, this Essay was appearing in *THE LANCET*, I have had the opportunity of trying the sedative effect of a weak solution of the glycerine spirit extract of the bean in water in a sufficient number of cases of strumous corneitis, both with and without ulceration of the cornea, where the irritation and photophobia have been considerable, and the eyes so susceptible that almost every other application caused distress; and also in those troublesome cases of inflamed lids in like constitutions, with such decided relief, that I think I may with some degree of confidence, speak of it as being of considerable value in those conditions of the eye where allaying irritation is of importance.

I have dropped the glycerine solution mixed with water into the eye two or three times a day, the patient almost always speaking of the application as being soothing and pleasant.

With regard to the best preparation and the best method of applying it, that one must be selected which will keep unchanged, and which admits of application to the conjunctiva without causing irritation; for in all cases the application should, I think, be made to this membrane. As the watery infusions and extracts will not keep, and are not so active as the spirituous preparations, they are not likely to be so much employed as them; perhaps, if the bean becomes abundant, an infusion may be used as a collyrium.

It will be seen that ether, chloroform, and acids are not good menstrua, as they possess the double disadvantage of not extracting much of the active principle of the bean, and also of irritating the eye when put into it. Their employment may be dismissed as injudicious. Boiling spirit extracts in the greatest degree the active principle; but then it is necessary to either drive off the whole of the spirit, or to so dilute this that when applied it shall not stimulate the conjunctiva. To preserve the extract and dilute it for use, glycerine has been employed. Messrs. Bell and others* have enclosed this glycerine solution in capillary tubes, hermetically sealed, in which it will probably keep unchanged for any length of time. So prepared, the application is easy, by breaking off both ends of the tube and blowing out the contents into the eye; but, as the quantity put in cannot always be accurately controlled, this is an objection to the method.

I have kept the spirit extract dissolved in glycerine for upwards of four months; it is apparently unchanged, and if it so continues, as it probably will do, this forms one of the most convenient preparations. The quantity and strength may be regulated with the greatest nicety, and the glycerine is a bland medium, and very miscible with other fluids if it be wished to use it in combination or greatly diluted.

Mr. Squire and Messrs. Bell and Co. have prepared paper saturated with a tincture of the bean, and then dried like the atropine paper suggested by Mr. Streatfeild. This is a very convenient form of preparation, and should it be found to keep unimpaired, of which I have some doubt (though experience alone can determine this point), it will, from its portability, be most commonly used, when simple temporary closure of the pupil is desired. A morsel of the paper should be put within the

* Mr. Reynolds, of Leeds, informs me that it was his idea and not Messrs. Bell and Co's to enclose the glycerine solution in capillary tubes as a means of preserving it. Had this preparation been liable, like the watery infusion and extract, to undergo speedy decomposition, the plan would have been valuable, but as it is now, I think, sufficiently proved that it keeps well, I do not see any great advantage in the method.

lower lid. The principal objection which I have found to the paper is, that in some eyes it acts as a foreign substance, particularly if it be not carefully and smoothly put in. It then causes a copious flow of tears, and, being carried about by the motion of the lids, is so soon washed out that the effect is lost. I have seen the paper remain in for forty-eight hours without exciting the least irritation; and I have known it washed out in a few minutes. In one case I have known it remain in for fourteen days, and in another for twenty-one days. The thinner the paper the better it is; hence I prefer that prepared by Mr. Squire, which is not more than half as thick as that made by Messrs. Bell and Co.

If the sedative effect of the bean be desired, one or other of the liquid preparations should be used. Mr. Squire has supplied me with a tincture of the bean. This is an elegant and persistent preparation, but which requires considerable dilution in its use, lest the spirit prove injurious. One drop to ten drops of water will, in many cases, act efficiently. If a permanent action be required, whatever the preparation used may be, unless, perhaps, in a less degree the paper, repetition of the application, at intervals of eight or twelve hours, is necessary in all cases. I have found the effect in twelve hours very considerably lessened, and in twenty-four, nearly if not altogether gone. The frequent repetition does not appear to be in any way prejudicial, nor the effect to be weakened. I have kept the irides of men and animals in a constant state of contraction for days and weeks, and in one boy for upwards of a month.* On the cessation of the application the pupil at once resumed its normal condition.

Whether any other substance possesses similar control over the iris remains to be proved: probably others will be found to act similarly.

As opium taken internally has the effect of contracting the pupil, I have tried its local action by dropping into the eye a solution of the acetate of morphia. A good deal of lachrymation, but not much contraction of the pupil, was induced, presenting thus a striking contrast to the Calabar bean; for while this, applied locally, contracts the pupil intensely, when taken internally, even to a fatal dose, it has comparatively little influence over it. Opium, on the other hand, taken internally, contracts the pupil strongly; applied locally, it appears to have little effect on it.

It has been stated that conia and Calabar bean have analogous actions. I have lately tried the effect of conia, locally and internally, without confirmation of the statement. My previous experience of the action of conia when administered by the mouth or lungs had not led me to consider the symptoms induced by Calabar bean like those caused by

* I have this day (Nov. 10th) seen this boy. His case was one of those alluded to in my paper of July 18th. The pupil is round, central, and contractile, forming the most successful cure I ever saw after a corresponding injury.

a poisonous dose of eonia.* In the latter the action is much more speedy: there is eonia, preceded by intense giddiness; consciousness and sensation are lost; and convulsions not unfrequently are caused,—none of which occur in Calabar bean poisoning. When eonia is put into the eye great lachrymation, irritation, and photophobia are induced, but no contraction of the pupil.

Mr. Reynolds suggested theine, and kindly supplied me with some for experiment. On trial, I find the result altogether negative.

Mr. Squire having sent me a supply of the extract of the flowering plant of acouite, I have tried it. It dilates the pupil less actively than belladonna, but with more irritation.

During the time this essay has been in course of publication I have had the opportunity of using the extract of the bean in the following case:—

In a child three weeks old, who has been suffering from acute purulent ophthalmia, from within a few days after birth, I found a considerable portion of both corneæ in a state of slough, through which a very large portion of the irides prolapsed. A solution of the spirit extract of the Calabar bean was put into both eyes, night and morning, for two days, when the prolapsed portions had greatly receded. The extract was now suspended for two days, at the end of which time the prolapsed portions had so greatly increased in size that the employment of it was resumed at once. The escaped parts again began to recede, and the corneal wounds to lessen, until, at the expiration of seven days, the ulcers had so nearly healed that the use of the bean was omitted. During this period the extract was dropped into the eyes twice daily; and as there was still some purulent discharge, a weak solution of nitrate of silver was also employed twice a day,—the two preparations being used alternately, at as nearly equal intervals of time as possible. The case is still under observation, and though it would be improper from a single case to make any very positive assertions as to cause and effect, I may with confidence state that I never saw a case in which the prolapse so completely and quickly withdrew and the corneal ulcers closed. Though the *propter hoc* may possibly not be proved, of the fact of the receding of the irides on the first application of the extract, of the renewed prolapse on the intermission of the application, and of the again speedy withdrawal of the escaped portions and healing of the ulcers on the renewed application, neither the intelligent surgeon whose patient the child was, and who himself kindly undertook to put the extract into the eyes to secure its

* See my paper in the "Transactions of the Provincial Medical and Surgical Association for 1849,"—"On Anæsthesia and Anæsthetic Substances generally: being an Experimental Inquiry into their Nature, Property, and Uses, &c."

being efficiently done, has, any more than myself, the slightest doubt. Should experience confirm my anticipations, I need hardly say that a most valuable remedy is discovered for assisting us in mitigating a dreadful calamity ; for, by the speedy withdrawal of the escaped iris from the wound, there is a much greater probability of a useful pupil being left ; and also, as the principal cause of irritation (the prolapsed iris) is removed, the inflammation quickly subsides and the corneal opening closes.

While this Essay has been in course of publication in the pages of THE LANCET, Dr. Robertson, of Edinburgh, has directed my notice to a paper,* in which, soon after the power which the bean possesses over the iris was discovered, he suggested, on theoretical grounds, that the use of it might be found beneficial in ulcers of the cornea, where there is a tendency of the iris to escape, but I find that he, like myself, had unknowingly been anticipated in the idea by Dr. Fraser in his thesis. Neither of these gentlemen, however, appears to have done more than suggest the possibility of the bean being found useful when so employed, and I feel assured that both of them will willingly concede that I may claim priority in the practical employment of the bean, as pointed out in my former paper, in wounds of the cornea, as well as in the various other affections I have alluded to in this essay.

LEEDS, 1863.

* The Calabar Bean as a New Ophthalmic Agent. By D. Argyll Robertson, M.D.

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MR. PERBURY, COFF OF TUMDUG

Engraved by J. H. B. from a drawing by J. H. B.



MR. J. H. HOPKINS, CASE OF THE TUMOR



M^{re} SPENCE'S CASE OF TUMOUR



MISS FENCES. CAST OF TUMOUR

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